PB88-173653

Health and Environmental Effects Profile for Dichloropropanes

(U.S.) Environmental Protection Agency
Cincinnati, OH

Sep 85

U.S. Department of Commerce
National Technical Information Service
NTIS

PB88-173653

EPA/600/X-85/360
September 1985

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR DICHLOROPROPANES

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

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U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA 22161

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA/600/X-85/360	2.	3. RECIPIENT'S ACCESSION NO.
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Dichloropropanes		5. REPORT DATE September 1985 6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS		10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268		13. TYPE OF REPORT AND PERIOD COVERED 14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES		

16. ABSTRACT

The Health and Environmental Effects Profile for dichloropropanes was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Dichloropropanes has been evaluated as a carcinogen. The human carcinogen potency factor (q_1^*) for dichloropropanes is 6.33×10^{-2} $(mg/kg/day)^{-1}$ for oral exposure.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for dichloropropanes is 1000.

17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 90
	20. SECURITY CLASS (This page) Unclassified	22. PRICE A05 14.95

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1984.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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LIST OF ABBREVIATIONS

BCF	Bioconcentration factor
BOD	Biological oxygen demand
BODT	Biological oxygen demand, theoretical
bw	Body weight
CAS	Chemical Abstract Service
CNS	Central nervous system
CODT	Chemical oxygen demand, theoretical
CS	Composite score
DNA	Deoxyribonucleic acid
EC_{50}	Median effective concentration
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
MATC	Maximum acceptable toxicant concentration
MED	Minimum effective dose
NADPH	Nicotinamide adenine dinucleotide phosphate
NOAEL	No-observed-adverse-effect level
NOEC	No-observed-effect concentration
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
RNA	Ribonucleic acid
RQ	Reportable quantity

LIST OF ABBREVIATIONS (cont.)

RV_d	Dose-rating value
RV_e	Effect-rating value
SCE	Sister-chromatid exchange
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
STEL	Short-term exposure level
TLV	Threshold limit value
TWA	Time-weighted average
UV	Ultraviolet
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The structures, CAS Registry numbers, molecular weights and empirical formulas of the dichloropropanes are presented in Table 1-1.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

The dichloropropanes are soluble in alcohol, ether, benzene and chloroform (Weast, 1980) and are liquids at room temperature. Available physical properties of the dichloropropanes are listed below:

1,1-Dichloropropane

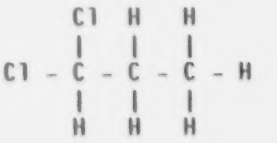
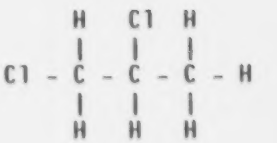
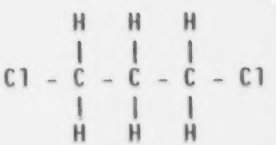
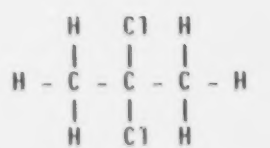
Boiling point:	88.1°C	Weast, 1980
Specific gravity:	1.1321 (20/4°C)	Weast, 1980
Refractive index:	1.4289 (20°C)	Weast, 1980
Log K_{ow}:	2.34	U.S. EPA, 1980

1,2-Dichloropropane

Melting point:	-100°C	Mabey et al., 1981
Boiling point:	98.6°C	Mabey et al., 1981
Specific gravity:	1.156 (20/4°C)	Weast, 1980
Refractive index:	1.4394 (20°C)	Weast, 1980
Water solubility: at 20°C	2700 ppm	Verschueren, 1983
Vapor pressure:		
at 20°C	42 mm Hg	Mabey et al., 1981
at 25°C	50 mm Hg	Verschueren, 1983
Log K_{ow}:	2.02 (calculated)	U.S. EPA, 1980
	2.28 (calculated)	Callahan et al., 1979
Henry's Law Constant: (atm-m³/mol)	2.07×10^{-3}	Mackay and Yeun, 1983
	2.31×10^{-3}	Mabey et al., 1981
	2.9×10^{-3}	Hine and Mookerjee, 1975

TABLE 1-1

Structures, CAS Numbers, Molecular Weights and Empirical Formulas of Dichloropropanes

Synonyms	CAS Number	Molecular Weight	Empirical Formula	Structure
1,1-Dichloropropane propylidene dichloride	79-99-9	112.99	$C_3H_6Cl_2$	
1,2-Dichloropropane propylene dichloride	78-87-5	112.99	$C_3H_6Cl_2$	
1,3-Dichloropropane trimethylene chloride trimethylene dichloride	142-28-9	112.99	$C_3H_6Cl_2$	
2,2-Dichloropropane	594-20-7	112.99	$C_3H_6Cl_2$	

1,3-Dichloropropane

Melting point:	-99.5°C	Weast, 1980
Boiling point:	120.4°C	Weast, 1980
Specific gravity:	1.1876 (20/4°C)	Weast, 1980
Refractive index:	1.4487 (20°C)	Weast, 1980
Log K_{ow}:	2.00 2.00	Hansch and Leo, 1979 Valvani et al., 1981
Water solubility: at 25°C	2800 ppm	Valvani et al., 1981
Vapor pressure: at 25°C	18.25 mm Hg	Hine and Mookerjee, 1975
Henry's Law Constant: (atm-m^3/mol)	$1x10^{-3}$	Hine and Mookerjee, 1975

2,2-Dichloropropane

Melting point:	33.8°C	Weast, 1980
Boiling point:	69.3°C	Weast, 1980
Specific gravity:	1.1136 (20/4°C)	Weast, 1980
Refractive index:	1.4148 (20°C)	Weast, 1980

1.3. PRODUCTION DATA

1,2-Dichloropropane is manufactured by Dow Chemical in Freeport, TX and Plaquemine, LA (SRI, 1984); it is also produced by Olin Corp. (USITC, 1984). In addition to being produced as a purified end product, it is manufactured as a component of a soil fumigant mixture (D-D®) made by Shell Chemical in Deer Park, TX and Norco, LA (SRI, 1984). Dow Chemical also produces this soil fumigant mixture (USITC, 1984). 1,3-Dichloropropane is not listed in either SRI (1984) or USITC (1984) as a commercially produced chemical, but may be present as a by-product in the soil fumigant mixture (U.S. EPA, 1981). 1,1-Dichloropropane is apparently not produced on a commercial scale.

TABLE 1-2

Production Data Available from the Public Portion of the TSCA Production File for 1977*

Manufacturer	Location	1977 Production Range (lbs)
1,1-Dichloropropane	no listings	NA
1,2-Dichloropropane		
Olin Corp.	Brandenburg, KY	10-50 million
Dow Chemical	Freeport, TX Plaquemine, LA	50-100 million 10-50 million
BASF Wyandotte	Wyandotte, MI	confidential
Shell Chemical	Deer Park, TX Norco, LA	1-10 million 1-10 million
Jefferson Chem.	Port Neches, TX	confidential
1,3-Dichloropropane		
Eastman Kodak	Rochester, NY	none
Columbia Organics	Columbia, SC	<1000
Shell Chemical	Norco, LA	1-10 million
2,2-Dichloropropane		
Columbia Organics	Columbia, SC	<1000

*Source: U.S. EPA, 1977

NA = Not applicable

Production data available from the U.S. EPA TSCA Production File for 1977 are listed in Table 1-2. In 1980, 77 million pounds of 1,2-dichloropropane were produced by Dow, Olin and BASF Wyandotte (USITC, 1981); this does not include Shell's production for the soil fumigant mixture.

1,2-Dichloropropane is produced by the chlorination of propylene (Hawley, 1977). The D-D® soil fumigant is also produced by the high temperature chlorination of propylene, but the reaction products are not isolated and the resultant product is a mixture of ~50% 1,3-dichloropropene and ~30% 1,2-dichloropropane, along with 3,3-dichloropropene, 2,3-dichloropropene and related C_3 chlorinated hydrocarbons (Hartley and Kidd, 1983; Martin and Worthing, 1977; Ouellette and King, 1977). Dow Chemical markets this mixture as Vidden D® and Telone®, while Shell markets it as D-D® (Ouellette and King, 1977). No data were located concerning production processes for the 2,2 isomer in the literature cited in the appendix.

1.4. USE DATA

The D-D® mixture is used in soil fumigation (Hartley and Kidd, 1983; Martin and Worthing, 1977) and is usually applied by injection into the soil or through tractor-drawn hollow tines, to a depth of 15-20 cm at 150-450 kg/ha depending on soil type and crop; the soil surface is sealed by rolling. In 1982 and 1976, 4.5 and 1.2 million pounds, respectively, of the D-D® mixture were used in the soil fumigation of tobacco fields (USDA, 1983); it is also used for soil fumigation of other crops.

1,2-Dichloropropane is used as an intermediate in the production of other chlorinated hydrocarbons, as a lead scavenger for antiknock fluids, as a solvent for fats, oils, waxes, gums, resins and cellulose esters and ethers, as a metal degreasing agent, as an extractant and in the preparation of cleaning and spot-removing compounds (Hawley, 1977; Kuney, 1984).

1,3-Dichloropropane is used as an alkylating and cyclyzing agent, and as a polymerization catalyst or promotor (U.S. EPA, 1981). No data were located concerning the 2,2 isomerin the literature cited in th appendix.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

The fate of the dichloropropanes in the environment depends upon their capacity to undergo chemical, photochemical, and biological alterations and to transport or partition from one environment matrix into another. The individual fate processes in water, air and soil are discussed below.

2.1. WATER

2.1.1. Hydroylsis. No environmentally relevant kinetic data regarding the hydrolysis of the dichloropropanes were located. Dilling et al. (1975) showed that the half-lives, with respect to hydrolysis, for various one- and two-carbon chloroaliphatics are 6 months to several years. Mabey et al. (1981) suggested that the neutral hydrolysis of 1,2-dichloropropane is on the same order of magnitude as that of chloroethane, which has a half-life at 25°C of ~40 days. Chloropropane has a neutral hydrolysis half-life at 25°C of 69 days (Mabey and Mill, 1978). The dichloropropanes may be expected to have similar rates for uncatalyzed hydrolysis.

2.1.2. Oxidation. Mabey et al. (1981) estimated the following aquatic oxidation rate constants for 1,2-dichloropropane:

for $^1O_2$ (singlet oxygen): $<<360\ M^{-1}\ hr^{-1}$

for RO_2 (peroxy radical): $\sim 1\ M^{-1}\ hr^{-1}$

Assuming $^1O_2$ and RO_2 concentrations of 10^{-12} and 10^{-9} M, respectively, in natural sunlit waters (Mabey et al., 1981), these oxidants have no significance in removing 1,2-dichloropropane from water. Dilling et al. (1975) also found that the aqueous oxidation of methylene chloride, chloroform, trichloroethane, trichloroethylene and tetrachloroethylene apparently was not an important transformation process. Therefore, oxidation of the dichloropropanes in the aquatic environment is judged to be not significant.

Small doses of ozone (0.01 mg ozone/mg compound) readily oxidized 1,2-dichloropropane in water (Medley and Stover, 1983). Therefore, if ozonation is used during treatment of water, complete oxidation of the compound may be feasible.

2.1.3. Photolysis. Data specific to the direct or photosensitized environmental photolysis of the dichloropropanes were not located. Although no supporting experimental data are available, Callahan et al. (1979) suggested that direct photolysis is not likely to be an important aquatic fate process for 1,2-dichloropropane because it does not have any chromophores that will absorb appropriate UV radiation. 1,3-Dichloropropane will undergo photolysis when exposed to radiation <290 nm (U.S. EPA, 1981), but this is not environmentally important.

2.1.4. Microbial Degradation. Stover and Kincannon (1983) performed a 5-day BOD test with a bench-scale activated sludge reactor and found 1,2-dichloropropane removal to be ~99%.

Tabak et al. (1981) examined the biodegradability of 1,2-dichloropropane with a static-culture, flask-screening procedure using settled domestic wastewater as a microbial inoculum. 1,2-Dichloropropane was found to be significantly biodegradable with a gradual adaptation; at a 5 ppm concentration, 42% was lost in 7 days and 89% was lost in 28 days.

Bridie et al. (1979a) tested the degradability of 1,3-dichloropropane in a 5-day BOD test using a filtered effluent from a wastewater treatment plant; a BODT and CODT of 17 and 74%, respectively, were observed. Kawasaki (1980) used the Japanese MITI test and concluded that 1,2-dichloropropane is degradation resistant. Thom and Agg (1975) reported that 1,2-dichloropropane should be degradable by biological sewage treatment provided proper acclimatization is achieved.

Mabey et al. (1981) estimated the bacterial transformation rate for 1,2-dichloropropane in the natural aquatic environment to be ~1×10^{-10} mℓ/cell-hr. Active bacterial populations in typical natural waters are ~10^4 to 10^5/mℓ for ponds, streams and eutrophic lakes (Lyman et al., 1982). These figures suggest that bacterial degradation of 1,2-dichloropropane in natural waters is initially slow and not significant. The rate of bacterial degradation, however, may increase by several orders of magnitude, assuming that the bacteria adapts to the dichloropropane.

2.1.5. Transport Processes.

2.1.5.1. VOLATILIZATION -- Based on experimental laboratory data, the volatilization of 1,2- and 1,3-dichloropropane from natural bodies of water appears to be a major mechanism in determining their fate in the environment. Chiou et al. (1980) measured the evaporation of 1,2-dichloropropane (1 ppm) from a 1.6 cm deep water solution under stirring; a half-life of 8 minutes was observed. Mackay and Yeun (1983) measured the volatilization of 1,2-dichloropropane from a wind-wave tank at 20°C and determined mass transfer coefficients at varying wind speeds; a half-life of 5.4 hours can be calculated from the data at a 1 m depth and 7 m/sec wind speed. Hine and Mookerjee (1975) measured the equilibrium water-to-air ratios of 1,2- and 1,3-dichloropropane at 25°C in dilute aqueous solution to be ~8 and 24, respectively; these ratios can be translated into Henry's Law Constants of 0.0029 and 0.001 atm-m³/mol, respectively. Henry's Law Constants of 0.00231 (Mabey et al., 1981) and 0.00207 (Mackay and Yeun, 1983) atm-m³/mol were reported for 1,2-dichloropropane. These values of Henry's Law Constants suggest that volatilization of 1,2- and 1,3-dichloropropane from natural bodies of water is significant and may be rapid (Lyman et al., 1982).

Using the U.S. EPA EXAMS computer simulation (Burns et al., 1981) and a Henry's Law Constant of 0.00231 atm-m³/mol, the following volatilization half-lives are computed for typical bodies of water containing 1,2-dichloropropane:

pond	1.7 days
eutrophic lake	10 days
oligotrophic lake	11 days
river	1.6 days

2.1.5.2. **ADSORPTION** -- Based on the estimated K_{oc} of 51 for 1,2-dichloropropane (Mabey et al., 1981), adsorption of the dichloropropanes to particulate organic matter and sediment in the aquatic environment does not appear to be important, although experimental data are not available. U.S. EPA (1980b) developed pulverized activated carbon absorption isotherm data for 1,2-dichloropropane. These data were developed in an effort to evaluate treatment capabilities of activated carbon. Data were fited to the Freundlich equation:

$$\log X/M = \log K + 1/n \log C_f$$

where:

$X=C_o-C_f$ the amount of compound absorbed

M=the weight of the activated carbon

C_o=the amount of compound in the untreated solution

C_f=the amount of compound remaining in the water

The empirical coefficients K and 1/n were estimated to be 5.86 and 0.60, respectively at ph 5.3. THe relevence of these data to sod absorption is

uncertain. Section 2.3.5 provides additional relevant data based on soil leaching studies.

2.1.5.3. **BIOACCUMULATION** -- The only available experimental data for the bioaccumulation potential of the dichloropropanes were reported by Jernelov et al. (1972). Shrimp were placed in a static system containing 2 ppm 1,3-dichloropropane; after 96 hours of exposure, the BCF was ~90. Using the MITI test, Kawasaki (1980) measured a BCF of ~10 in fish exposed to 1,2-dichloropropane.

The BCF of an organic compound may be predicted from the K_{ow} using the following equation developed by Veith et al. (1980): Log BCF = 0.76 Log K_{ow}-0.23. For both 1,2- and 1,3-dichloropropane, Log K_{ow} is ~2.00 (see Section 1.2.); therefore, the BCF value is calculated to be ~20. The BCF may also be predicted from the WS using the Kenaga and Goring (1980) equation: Log BCF = 2.791-0.564 Log WS. For 1,2- and 1,3-dichloropropane, the WS is 2700 and 2800 ppm, respectively (see Section 1.2.); therefore, the BCF value is calculated to be ~7. U.S. EPA (1980) also estimated BCF values of 19.4, 10.4 and 10 for 1,1-dichloropropane, 1,2-dichloropropane and 1,3-dichloropropane, respectively. These BCF values indicate that bioaccumulation of the dichloropropanes in aquatic organisms is not a significant process.

2.2. AIR

Experimental data regarding the fate of the dichloropropanes in air were not located in the available literature cited in the Appendix. The rate constant for the reaction between hydroxyl radicals and the dichloromethanes and ethanes is ~10^{13} cm^3/mol-sec (Lyman et al., 1982). Assuming that this rate constant is valid for the dichloropropanes and that the average atmospheric concentration of hydroxyl radicals is 10^{-18} mol/cm^3, a half-life of ~80 days can be calculated. In moderately polluted atmospheres, the

hydroxyl radical concentration may be a factor of 10 higher, yielding a half-life of only 8 days.

In air, the removal of dichloroprophanes through physical processes may not be significant in determining their fate. 1,2-Dichloropropane and 1,3-dichloropropane have dissolution (wet deposition by rainfall) half-lives of ~1 year based on the Cupitt (1980) method. The volatility of these compounds suggests, however, that once dissolved, they will revolatilize rapidly.

2.3. SOIL

2.3.1. Microbial Degradation. Altman and Lawlor (1966) found that various bacteria that can be isolated from soil can grow abundantly in media using 100 ppm 1,2-dichloropropane as a sole carbon source. The bacteria include Rhizobium legumunosarum, Bacillus subtilus, Azotobacter vinelandii, Arthrobacter globiformis, Pseudomonas flurorescens, Corynebacterium fascians and C. insidiosum. The Arthrobacter and Bacillus species also grew at a concentration of 1000 ppm 1,2-dichloropropane.

Altman (1969) and Dubey et al. (1975) found that soil microorganisms are capable of using D-D® mixture as a sole carbon source. The D-D® mixture contains 1,3-dichloropropene and other C_3 chlorohydrocarbons in addition to 1,2-dichloropropane.

Roberts and Stoydin (1976) added ^{14}C-2-labeled 1,2-dichloropropane (45-74 mg/kg) to a sandy loam soil and to a medium loam soil in glass containers. The containers were sealed and incubated in the dark at 20-22°C. Less than 0.2% of the applied radioactive material degraded in the sandy loam and in the medium loam after 80 and 20 weeks incubation, respectively. In contrast to the pure culture studies, these results suggest that very little degradation occurred utilizing soil media under the conditions of the is experiment.

Consequently, additional data are required to accurately establish the importance of microbial degradation of 1,2-dichloropropane in the natural soil environment (Dynamac Corporation, 1982). No soil microbial degradation data were located for 1,1- or 1,3-dichloropropane.

2.3.2. Chemical Degradation. Pertinent data regarding the chemical hydrolysis or oxidation of the dichloropropanes in soil were not located in the available literature cited in the Appendix.

2.3.3. Photolysis. Pertinent data regarding the photolysis of the dichloropropanes in soil surfaces were not located in the available literature cited in the Appendix.

2.3.4. Volatilization. Roberts and Stoydin (1976) examined the volatility of ^{14}C-2-labeled 1,2-dichloropropane from a sandy loam soil under simulated conditions. Ten days after application of the 1,2-dichloropropane, <1% of the original radiolabel remained in the soil because of volatilization. This suggests that volatilization of 1,2-dichloropropane is probably the dominant fate process in soil. Data specific to 1,1- or 1,3-dichloropropane were not located, but the high vapor pressure of 1,3-dichloropropane suggests that its evaporation may be expected to be significant and as rapid as the 1,2-isomer.

2.3.5. Adsorption -- Leaching. Chiou et al. (1979) examined the absorption of 1,2-dichloropropane in a silt loam soil (1.6% organic matter, 26% clay, 3.3% sand and 69% silt) by determining soil-water equilibrium isotherms at 20°C. The relationship of soil uptake vs. equilibrium concentration was linear, suggesting that uptake of nonionic organic compounds is essentially a result of the solute partitioning into soil organic matter rather than physical adsorption. The K_{oc} for 1,2-dichloropropane was determined to be 27, indicating high soil mobility.

The K_{oc} value of an organic compound may be estimated from the WS using the following equation developed by Kenaga and Goring (1980): Log K_{oc} = 3.64-0.55 Log WS. For 1,2- and 1,3-dichloropropane, WS is ~2700 ppm; therefore, the K_{oc} value is calculated to be ~57. Prediction from molecular topology and quantitative structure-activity relationship yields a K_{oc} value for the dichloropropanes of ~50 (Sabljic, 1984). Both of these results suggest that the two dichloropropanes may not be sorbed strongly to soils.

2.3.6. Persistence. The persistence of the dichloropropanes in soil under field conditions has not been reported; however, initial dissipation is likely to be rapid due to volatilization. Van Dijk (1980) studied the dissipation rate of 1,2-dichloropropane in sealed glass containers that effectively limited the volatility mechanism. In four soil types (two sandy and two clay) the dissipation half-life at 15°C ranged from 41-69 days. While the dissipation mechanism was not discussed in detail, it apparently involved either microbial or chemical degradation or a combination of both. These half-lives suggest that, in the absence of volatility, 1,2-dichloropropane may persist in soil.

2.4. SUMMARY

Most of the data available regarding the environmental fate of the dichloropropanes is specific to 1,2-dichloropropane. Some experimental data and data from predictive theories are available for the two other chloropropanes.

Volatilization appears to be the dominant process determining the fate of dichloropropanes in both water and soil. Once exposed to the ambient atmosphere, the dichloropropanes appear susceptible to oxidation by hydroxyl radicals. Although kinetic rate data specific to the dichloropropanes are

not available, data are available for hydroxyl radical reactions with one- and two-carbon chloroaliphatics.

The ability of the dichloropropanes to be degraded significantly by microbes in the natural environment is not certain because additional experimental data are required. Hydrolysis, oxidation and direct photolysis in the aquatic environment do not appear to be significant fate processes. The dichloropropanes are not expected to bioaccumulate strongly in aquatic organisms. 1,2-Dichloropropane and 1,3-dichloropropane appear susceptible to significant leaching in soil.

3. EXPOSURE

3.1. WATER

Dichloropropane can enter the aquatic environment through discharges from industrial and manufacturing processes, run-off from agricultural lands and from municipal effluents (U.S. EPA, 1980).

1,2-Dichloropropane and unspecified isomers of dichloropropane have been detected in finished drinking water, well water, effluents from chemical plants and sewage treatment plants, river water and seawater (Shackelford and Keith, 1976).

Westrick et al. (1984) reported the results of the U.S. EPA Groundwater Supply Survey, which examined the finished waters from 945 water supplies throughout the United States. The results for 1,2-dichloropropane are listed in Table 3-1.

Cole et al. (1984) reported preliminary results of the U.S. EPA Nationwide Urban Runoff Program, which measured urban stormwater runoff for the presence of priority pollutants. In 86 water samples examined from 15 cities, 1,2-dichloropropane was detected only once in Eugene, OR at a level of 3 µg/ℓ.

Dowty et al. (1975) detected dichloropropane (isomer or concentration not reported) in bottled artesian water from New Orleans, LA. 1,2-Dichloropropane and 1,3-dichloropropane have been identified in Ohio River water and its tributaries at levels up to 0.8 ppb (Ohio River Valley Water Sanitation Commission, 1979, 1980). Dewalle and Chian (1978) measured 1,2-dichloropropane levels >1 ppb in Delaware River water and its tributaries, while Dreisch et al. (1980) found trace levels in Ohio River water in Huntington, WV. Piet and Morra (1979) found maximum levels of 300 ng/ℓ in tap water in the Netherlands, which underwent bank filtration from the Rhine River,

TABLE 3-1

1,2-Dichloropropane Occurrences and Concentrations Found in the Groundwater Supply Survey[a]

No. of Sites	No. of Occurrences	Concentration (µg/ℓ)	
		Median	Maximum
280 random sites[b]	1	0.75	0.75
186 random sites[c]	5	0.96	21
321 nonrandom sites[b]	3	1.2	1.4
158 nonrandom sites[c]	4	0.7	18

[a]Source: Westrick et al., 1984

[b]Serves <10,000 people

[c]Serves >10,000 people

while Zuercher and Giger (1976) detected 1,2-dichloropropane (no levels reported) in Glatt River water in Switzerland.

Ewing et al. (1977) analyzed surface waters from 14 heavily industrialized river basins in the United States and found 1,2-dichloropropane in 5 of 204 sites sampled at levels of ~1-2 ppb. 1,2-Dichloropropane has been detected at levels <10 mg/ℓ in effluents from the petroleum refining industry (Snider and Manning, 1982) and in wastewaters generated by the Oak Ridge Gaseous Diffusion Plant in Tenessee (McMahon, 1983). Rawlings and Samfield (1979) monitored raw wastewater and secondary effluent from 32 textile plants in the United States for 12 priority pollutants. 1,2-Dichloropropane was detected in one raw wastewater sample at a concentration of 2 ppb. Barkley et al. (1980) detected dichloropropane (isomer not reported) at a level of 1.2 ppm in the drinking water of a household located near the Love Canal area in Niagara, NY.

The gross analyses for 1,2- and 1,3-dichloropropane available from the U.S. EPA STORET data base are listed in Table 3-2.

3.2. FOOD

Pertinent data regarding the concentration or occurrence of dichloropropanes in commercial or ready-to-eat foods were not located in the available literature as cited in the Appendix.

3.3. INHALATION

The dichloropropanes may enter the ambient atmosphere as a result of industrial emissions or volatilization from their use as soil fumigants and solvents. Volatilization from contaminated waters is also another source of atmospheric dichloropropanes.

TABLE 3-2

STORET Data Base Gross Analyses

	Water	Sediment (dryout)	Fish Tissue
1,2-Dichloropropane			
No. observations	22,670	666	556
Max. Concentration	25,000 µg/ℓ	580 µg/kg	25.0 mg/kg
Min. Concentration	0 µg/ℓ	0 µg/kg	0 mg/kg
Mean Concentration	10 µg/ℓ	12.7 µg/kg	0.8 mg/kg
1,3-Dichloropropane			
No. observations	34	NR	NR
Max. Concentration	3.0 µg/ℓ	NR	NR
Min. Concentration	1.0 µg/ℓ	NR	NR
Mean Concentration	1.2 µg/ℓ	NR	NR

NR = Not reported

Brodzinsky and Singh (1982) compiled United States air monitoring data for >150 organic compounds. 1,2-Dichloropropane was detected in 396 air samples from urban/suburban ambient atmospheres at a mean concentration of 57 ppt; 26 samples from the vicinity of point sources of contamination had a mean concentration of 120 ppt. Pellizzari (1982) detected levels of 1-2 $\mu g/m^3$ (0.2-0.4 ppb) of 1,2-dichloropropane in the air near industrial chemical plants near Baton Rouge, LA; Pellizzari et al. (1979) previously reported levels of 0-40 ppb in the same vicinity.

Singh et al. (1981) monitored the air in St. Louis, MO; Denver, CO and Riverside, CA during May-July, 1980 and detected average 1,2-dichloropropane concentrations of 53, 48 and 57 ppt, respectively. Additionally, Singh et al. (1982) monitored the air in Houston, TX; Staten Island, NY; Pittsburgh, PA and Chicago, IL and found average 1,2-dichloropropane concentrations of 79, 25, 22 and 28 ppt, respectively. Barkley et al. (1980) found trace levels of 1,2-dichloropropane outside of homes near the Love Canal in Niagara Falls, NY.

1,3-Dichloropropane has been detected (no concentration reported) in the air surrounding the brominated chemical industry in Arkansas (DeCarlo, 1979). Graedel (1978) reported that 1,3-dichloropropane has been detected at levels of 2 ppb in ambient air near industrial sites.

3.4. DERMAL

Pertinent data regarding the dermal exposure of the dichloropropanes were not located in the available literature as cited in the Appendix.

4. PHARMACOKINETICS

Pertinent data regarding the pharmacokinetics of 1,1-dichloropropane 2,2-dichloropropane and 1,3-dichloropropane were not located in the available literature as cited in the Appendix.

4.1. ABSORPTION

In a study on the excretion of 1,2-dichloropropane (Section 4.4.), rats were treated by gavage with 1,2-dichloro(1-^{14}C)propane in arachis oil at 0.88 mg/rat (Hutson et al., 1971). Within 24 hours, ~50% of the administered radioactivity was recovered in the urine and only ~4.5% in the feces. After 96 hours, urinary recovery was ~53% and fecal recovery was ~6%; in the GI tract, 0.5% of the radioactivity was found. In a separate experiment, 42.4% of the administered dose of radioactivity was detected in the expired air of rats collected over 96 hours following a 1.07 mg/rat gavage dose of ^{14}C-1,2-dichloropropane. Although the percentage of radioactivity in expired air after 24 hours was not reported, Hutson et al. (1971) stated that 80-90% of the administered radioactivity was excreted in urine, feces and expired air in 24 hours. These data indicated that 1,2-dichloropropane was absorbed rapidly and extensively by the GI tract of rats.

4.2. DISTRIBUTION

Data regarding the distribution and retention of 1,2-dichloropropane are limited. In the previously described study of Hutson et al. (1971) (see Section 4.1.), ~1.5% and 3.5% of the administered dose of radioactivity from ^{14}C-1,2-dichloropropane were found in the skin and carcass, respectively, of rats after 96 hours.

4.3. METABOLISM

Van Dyke and Wineman (1971) found that 5.8% of the chlorine atoms were enzymatically removed from [^{36}Cl]-1,2-dichloropropane after 30 minutes of incubation with microsomes, cytosolic enzymes and the NADPH-generating system.

Jones and Gibson (1980) studied the metabolism of 1,2-dichloropropane in rats *in vivo* and *in vitro*. The major urinary metabolite in rats treated by gavage with 1,2-dichloropropane at 20 mg/kg/day for 4 days was identified as the mercapturic acid, N-acetyl-S- (2-hydroxypropyl) cysteine. As determined by *in vitro* experiments, this metabolite was formed by the conjugation of a dechlorinated intermediate, 1,2-epoxypropane, with glutathione rather than by direct conjugation of glutathione with 1,2-dichloropropane or a chlorinated intermediate, 1-chloro-2-hydroxypropane. Based on *in vitro* experiments, 1-chloro-2-hydroxypropane and 1,2-epoxypropane were also proposed as intermediates in the oxidation of 1,2-dichloropropane to propane-1,2-diol.

Oral administration of either 1,2-dichloropropane or 1-chloro-2-hydroxypropane to rats resulted in the excretion of common urinary metabolites, ß-chlorolactate and N-acetyl-S-(2,3-dihydroxypropyl) cysteine, the latter of which was thought to be a product of 3-chloropropan-1,2-diol by 2,3-epoxypropan-1-ol. 3-Chloropropan-1,2-diol is interconvertible with ß-chlorolactaldehyde, a urinary metabolite of 1-chloro-2-hydroxypropane. The metabolic pathway depicted in Figure 4-1 was proposed.

According to the scheme, 1,2-dichloropropane is dechlorinated and oxidized to 1-chloro-2-hydroxypropane, which is further dechlorinated to 1,2-expoxypropane. Epoxypropane can either react with glutathione to yield the mercapturic acid, N-acetyl-S-(2-hydroxypropyl) cysteine, which is

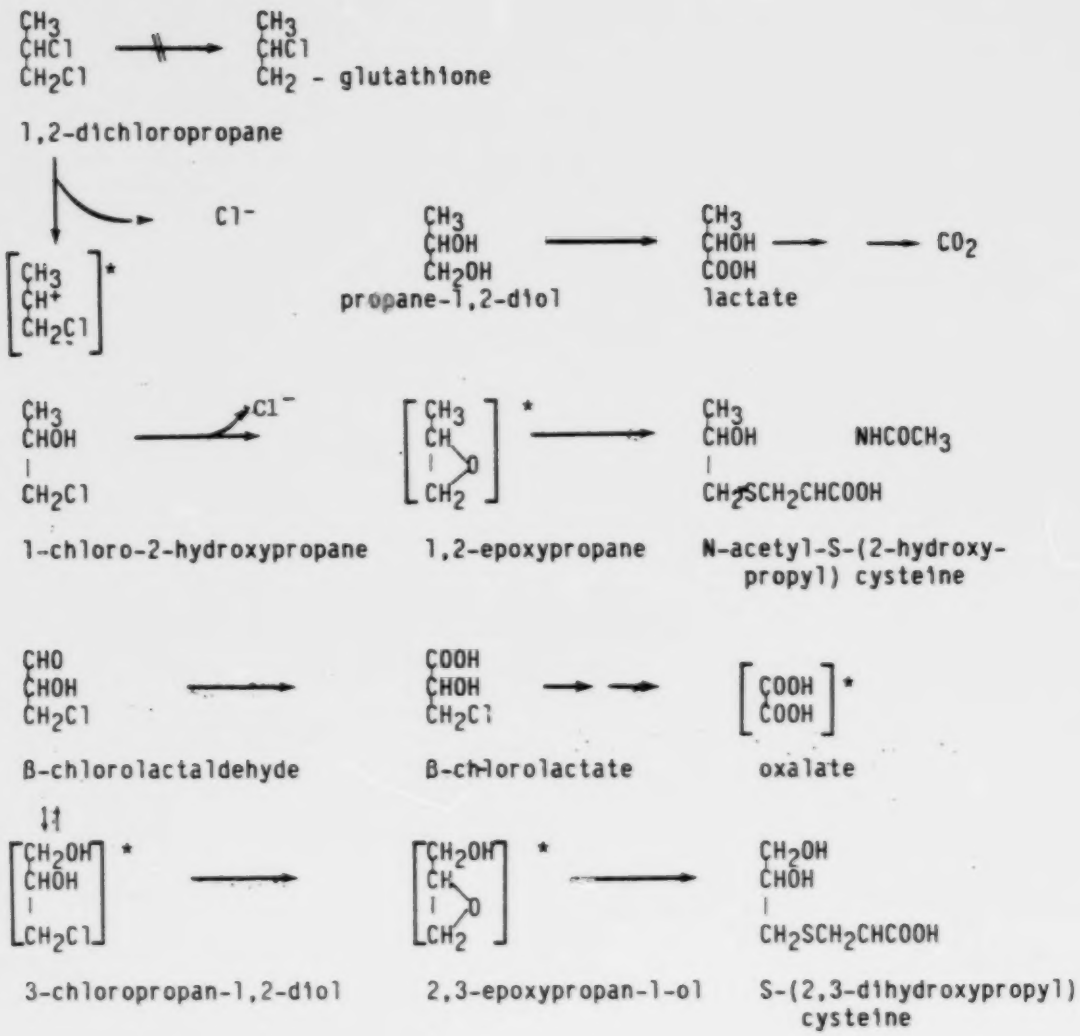


FIGURE 4-1

Proposed Metabolic Pathway for 1,2-Dichloropropane in the Rat

Source: Jones and Gibson, 1980

*Compounds in brackets are proposed intermediates

excreted in the urine, or be hydrolyzed to propane-1,2-diol, which is oxidized to lactate, which in turn is oxidized to pyruvate. Pyruvate can enter the tricarboxylic acid cycle, and CO_2 is liberated. As discussed in Section 4.1., Hutson et al. (1971) found that rats expired ~40% of the administered dose of radioactivity from ^{14}C-1,2-dichloropropane as $^{14}CO_2$. 1-Chloro-2-hydroxypropane can also be oxidized to β-chlorolactaldehyde, which can be further oxidized to β-chlorolactate and oxalate or be interconverted to 3-chloropropan-1,2-diol (Jones and Gibson, 1980). Epoxidation of the diol would yield 2,3-epoxypropan-1-ol, which can react with glutathione to yield S-(2,3-dihydroxypropyl) cysteine.

4.4. EXCRETION

Six Carworth Farm E strain rats (200-250 g) of each sex were dosed by stomach tube with a solution of 1,2-dichloro(1-^{14}C)propane (0.88 mg, 8.5 μCi) in 0.5 mℓ of arachis oil (Hutson et al., 1971). The excretion of radioactivity as percent of the administered dose was determined in the urine and feces at 24-hour intervals over a period of 4 days. Animals were sacrificed after 4 days and radioactivity remaining in the carcass was measured. In a separate experiment, female rats were dosed with 1.07 mg ^{14}C-1,2-dichloropropane and expired air was collected and analyzed for radioactive compounds. Of the administered radioactivity, 80-90% was eliminated in the first 24 hours, including radioactivity in expired air. In the urine of male rats, 48.5% of the administered dose was excreted after 24 hours; total urinary excretion was 51.1% after 96 hours. In females, urinary excretion was 51.9% after 24 hours and 54.4% after 96 hours. In males, 5.0% of the dose was found in feces in the first 24 hours with a total fecal excretion of 6.8% (±2.61%) after 96 hours. Females had a fecal excretion of 3.8% at 24 hours and 4.9% (±1.07) after 96 hours. After 96

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of dichloropropanes were available only for 1,2-dichloropropane.

Groups of 50 male and 50 female B6C3F1 mice and 50 female F344/N rats were treated by gavage with 1,2-dichloropropane (99.4%) in corn oil at doses of 0, 125 and 250 mg/kg/day, 5 days/week for 103 weeks (NTP, 1983). Groups of 50 male F344/N rats were similarly treated at 0, 62 or 125 mg/kg/day. Surviving rats were killed after 105-108 weeks; surviving mice were killed after 105-107 weeks. Gross and comprehensive histologic examinations were performed on all animals that died or were killed when moribund during the study or were killed at the end of the study, except when examination was precluded by cannibalism or autolysis.

For rats, survival was 39/50 for male controls, 42/50 for low-dose males, 41/50 for high-dose males, 37/50 for female controls, 43/50 for low-dose females and 16/50 for high-dose females. The survival of the high-dose female rats was significantly ($p<0.001$) lower than the control and low-dose groups.

As seen in Table 5-1, there was a significant ($p=0.005$) dose-related increased incidence of mammary gland adenocarcinomas in female rats. The incidence for the high dose group was significantly ($p=0.012$) higher than for the controls when analyzed by Life Table Analysis, which, because of the reduced survival, was a more meaningful statistical test than the Fisher's Exact Test for this group. An increased incidence of mammary gland hyperplasia was observed in low-dose females (20/50) compared with controls (10/50). The low incidence of mammary gland hyperplasia observed in the high-dose females (1/50) may have been due to the low survival and increased

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TABLE 5-1

Incidence of Tumors in Rats and Mice Following Oral Exposure to 1,2-Dichloropropane

Species/ Strain	Sex	Dose[b] (mg/kg/day)	Duration of Treatment (weeks)	Duration of Study (weeks)	Purity of Compound (%)	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence (p value)
rat/F344	F	0	103	105-108	>99.4	corn oil	mammary gland	adenocarcinoma	1/50 (p=0.005)[c]
		125	103	105-108	>99.4	corn oil	mammary gland	adenocarcinoma	2/50 (p=n.s.)[d]
		250	103	105-108	>99.4	corn oil	mammary gland	adenocarcinoma	5/50 (p=0.012)[e]
mouse/ B6C3F1	F	0	103	105-107	>99.4	corn oil	liver	adenoma	1/50 (p=0.029)[c]
		125	103	105-107	>99.4	corn oil	liver	adenoma	4/50 (p=0.041)[e]
		250	103	105-107	>99.4	corn oil	liver	adenoma	5/50 (p=0.013)[e]
mouse/ B6C3F1	F	0	103	105-107	>99.4	corn oil	liver	carcinoma	1/50 (p=n.s.)[d]
		125	103	105-107	>99.4	corn oil	liver	carcinoma	3/50 (p=n.s.)[d]
		250	103	105-107	>99.4	corn oil	liver	carcinoma	4/50 (p=n.s.)[d]
mouse/ B6C3F1	F	0	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	1/50 (p=0.005)[f]
		125	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	7/50 (p=0.030)[g]
		250	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	9/50 (p=0.008)[g]
mouse/ B6C3F1	M	0	103	105-107	>99.4	corn oil	liver	adenoma	7/50 (p=0.020)[c]
		125	103	105-107	>99.4	corn oil	liver	adenoma	10/49 (p=n.s.)[d]
		250	103	105-107	>99.4	corn oil	liver	adenoma	16/50 (p=0.028)[g]
mouse/ B6C3F1	M	0	103	105-107	>99.4	corn oil	liver	carcinoma	11/50 (p=n.s.)[d]
		125	103	105-107	>99.4	corn oil	liver	carcinoma	16/49 (p=n.s.)[d]
		250	103	105-107	>99.4	corn oil	liver	carcinoma	16/50 (p=n.s.)[d]
mouse/ B6C3F1	M	0	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	18/50 (p=0.003)[f]
		125	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	25/49 (p=n.s.)[d]
		250	103	105-107	>99.4	corn oil	liver	adenoma or carcinoma	32/50 (p=0.004)[g]

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TABLE 5-1

Species/ Strain	Sex	Dose[b] (mg/kg/day)	Duration of Treatment (weeks)	Duration of Study (weeks)	Purity of Compound (%)	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence (p value)
QUALITY OF EVIDENCE									
Strengths of Study: Both sexes of rats and mice were treated at two dose levels by a relevant route for their lifespan. Appropriate statistical analyses were performed. Comprehensive histologic examination were made.									
Overall Adequacy: Adequate									

[a]Source: NTP, 1983

[b]The chemical was administered 5 days/week.

[c]Significant positive dose-related trend by Life Table Analyses.

[d]Not significantly different from control by any statistical analyses.

[e]Significantly increase above control by Life Table Analyses.

[f]Significant positive dose-related trend by Cochran-Armitage Test.

[g]Significantly increased above control by Fisher's Exact Test.

n.s. = Not stated

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incidences of mammary gland adenocarcinoma in the group. The incidences of fibroadenoma were comparable among groups when analyzed by Life Table Tests. No significantly increased incidence of tumors occurred in male rats. It was concluded that there was no evidence that 1,2-dichloropropane was carcino- genic to male rats and the evidence in female rats was equivocal.

For mice, survival was 35/50 for control males, 33/50 for low-dose males, 35/50 for high-dose males, 35/50 for control females, 29/50 for low-dose females and 26/50 for high-dose females. Survival of low- and high-dose females was significantly ($p=0.035$) lower than control. Reduced survival of female rats may have been due to high incidences of infections of the reproductive tract.

As seen in Table 5-1, there were significant dose-related increased incidences of adenomas or carcinomas in the livers of males ($p=0.003$) and females ($p=0.009$). The incidences were significantly higher than the controls for the low- and high-dose females and for the high-dose males. When considered separately, the increased incidences of adenomas were significant, but the increased incidences of carcinomas were not. In addition to the liver tumors, there was a significant dose-related ($p=0.034$) increased incidence of follicular cell adenomas or carcinomas in female mice. The incidence was 1/48 for controls, 0/45 for low- and 5/46 for high-dose females, and was significantly greater than control for the high-dose females when analyzed by Life Table and Incidental Tumor Tests but not by the Fisher's Exact Test. The NTP (1983) was not certain if the thyroid tumor incidence was treatment-related because all the follicular cell tumors were found in the mice killed at the end of the study; a high rate of early deaths in the treated mice may have reduced the number at risk

for developing the tumor. It was concluded that the incidence of hepatocellular adenomas provided some evidence that 1,2-dichloropropane was carcinogenic to male and female mice. The increased incidence of hepatocellular carcinomas support the conclusion.

Heppel et al. (1948) repeatedly exposed 80 C3H mice to 400 ppm (1849 mg/m^3) of 1,2-dichloropropane for 4-7 hours/day for a total of 37 exposures. The mice were observed for 7 months. Only 3/80 mice survived and multiple hepatomas were seen in all three of the survivors.

5.2. MUTAGENICITY

Mutagenicity studies of dichloropropanes are summarized in Table 5-2. The majority of the testing has been performed with 1,2-dichloropropane; only one study on 1,3-dichloropropane and no studies on 1,1-dichloropropane were located in the available literature cited in the Appendix.

1,2-Dichloropropane has been tested for reverse mutation in Salmonella typhimurium strains TA100, TA1535, TA1537, TA98, TA1538 and TA1978 (NTP, 1983; Haworth et al., 1983; Principe et al., 1981; Carere and Morpurgo, 1981; DeLorenzo et al., 1977; Stolzenberg and Hine, 1980). Positive responses have been found only in TA100 and TA1535. NTP (1983) found marginally positive responses in TA100 and TA1535 in plate incorporation tests at concentrations $\geq$1000 µg/plate, while Haworth et al. (1983) found a marginally positive response only with TA100. In both studies, negative results were obtained when the S9 fraction was included in the incubation system. Principe et al. (1981) and DeLorenzo et al. (1977) found definite positive dose-related responses in these strains at concentrations of 1-50 mg/plate with and without S9, although the response was generally lower in the presense of S9 at $\leq$11 mg/plate (Principe et al., 1981). Stolzenberg and

TABLE 5-2

Mutagenicity Testing of Dichloropropanes

Assay	Indicator/ Organism	Dichloropropane	Applicator	Concentration or Dose	Activating System	Response	Comment	Reference
Reverse mutation	Salmonella typhimurium TA100 TA1535 TA1537 TA98	1,2-	plate incorporation	0-2000 µg/plate	+S9 -S9 +S9 -S9	± ± - -	There was a dose-related increase in the number of revertants/plate in TA100 and TA1535, with marginally positive responses at 1000 and 2000 µg/plate. In no case was the response ≥2 times the control response. S9 was prepared from Aroclor-induced rats and hamsters. Results were negative with S9.	NTP, 1983
Reverse mutation	S. typhimurium TA100 TA1535 TA1537 TA98	1,2-	plate incorporation	0-10,000 µg/plate	+S9 -S9 +S9 -S9	± - - -	There was a reproducible dose-related increase in the number of revertants/ plate at ≤6667 µg/plate in TA100. The increase was never ≥2 times the control. Results were negative with S9 from rats and hamsters.	Haworth et al., 1983
Reverse mutation	S. typhimurium TA1535 TA1537 TA1538 TA98	1,2-	plate incorporation	0, 10 µl/plate (0,11 mg/plate)	+S9 -S9 +S9 -S9	++ - - -	The response was ≥2 times the control in TA100 and TA1537 with and without S9. The response was greater in the absence of S9 ($p<0.01$) than in the presense of S9 ($p<0.05$).	Principe et al., 1981; Carere and Morpurgo, 1981
	TA100				+S9	++		
Reverse mutation	S. typhimurium TA1535 TA100	1,2-	plate incorporation	0, 1, 2.5, 5 and 10 µl/plate (≤11 mg/plate)	+S9 -S9	++ ++	Dose-related increases, ≥1 µl/plate in absence of S9; dose-related increases at ≥2.5 µl/plate in presence of S9. Responses were greater in the absence of S9.	Principe et al., 1981; Carere and Morpurgo, 1981
Reverse mutation	S. typhimurium TA1535 TA1978 TA100	1,2-	plate incorporation	0, 10, 20, 50 mg/plate	+S9 -S9 +S9	++ - ++	Dose-related increases; >2-fold increase above control in TA100 and TA1535 at all concentrations with and without S9.	DeLorenzo et al., 1977

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TABLE 5-2 (cont.)

Assay	Indicator/ Organism	Dichloropropane	Applicator	Concentration or Dose	Activating System	Response	Comment	Reference
Reverse mutation	S. typhimurium TA100	1,2-	plate incorporation	0, 1, 10 and 100 µmol/plate (≤11 mg/plate)	±S9	-	Complete inhibition of lawn growth at 100 µmol/plate	Stolzenberg and Hine, 1980
Reverse mutation	S. typhimurium TA100	1,3-	plate incorporation	0, 1, 10 and 100 µmol/plate (≤11 mg/plate)	±S9	++	No activity at 1 µmol/ plate	Stolzenberg and Hine, 1980
Forward mutation	Streptomyces coelicolor	1,2-	plate incorporation	0, 2, 10, 2, 100 µL/plate (<11 mg/plate	none	-	NC	Principe et al., 1981; Carere and Morpurgo, 1981
Forward mutation	S. coelicolor	1,2-	spot test	0, 100 µL/plate (0, 11 mg/plate)	none	-	NC	Principe et al., 1981
Forward mutation	Aspergillus nidulans	1,2-	plate incorporation	0, 100, 200, 300 and 400 µL/plate (≤44 mg/plate)	none	+	NC	Principe et al., 1981; Carere and Morpurgo, 1981
Forward mutation	A. nidulans	1,2-	spot test	0, 300 µL/plate (0, 33 mg/plate)	none	+	NC	Principe et al., 1981
SCE	Chinese hamster ovary cells	1,2-	cell culture	112.7-1127 µg/mL	±S9	++	NC	NTP, 1983
Chromosome aberrations	Chinese hamster ovary cells	1,2-	cell culture	460-1580 µg/mL	±S9	++	NC	NTP, 1983
Chromosome aberrations	rat bone marrow	1,2-	NR	NR	NR	+	NC	Dragusanu and Goldstein, 1975

NC = No comment; NR = not reported

Hine (1980), however, found that 1,2-dichloropropane at 0.11 and 1.1 mg/plate was negative for reverse mutations in S. typhimurium strain TA100, and at 11 mg/plate completely inhibited lawn growth.

1,2-Dichloropropane was negative for forward mutation in a test using Streptomyces coelicolor but positive in a test using Aspergillus nidulans in the absence of S9 (Principe et al. 1981; Carere and Morpurgo, 1981). Positive results were obtained for SCE and chromosome aberrations, with and without activation, in cultured Chinese hamster ovary cells (NTP, 1983) and for chromosome aberrations in rat bone marrow (Dragusanu and Goldstein, 1975).

1,3-Dichloropropane was tested for reverse mutation in S. typhimurium strain TA100 with positive results at concentrations of 1.1 and 11 mg/plate in the presence of S9 (Stolzenberg and Hine, 1980). These concentrations were also reported to be toxic to the bacteria. In the absence of S9, a positive response was obtained at 1.1 mg/plate, but a concentration of 11 mg/plate completely inhibited lawn growth.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of the dichloropropanes were not located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Shaipak (1976) reported that exposure to 9 mg/m³ of 1,2-dichloropropane for "long periods of time" impaired spermatogenesis in rats. No additional information was given in the abstract of this Russian study.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Pertinent data regarding the chronic and subchronic toxicity of 1,3- or 1,1-dichloropropane were not located in the available literature as cited in the Appendix.

The only information regarding the effects of long-term oral exposure of animals to 1,2-dichloropropane was found in the NTP (1983) bioassay. Groups of 50 male and 50 female F344/N rats and B6C3F1 mice were treated by gavage with 1,2-dichloropropane in corn oil for 103 weeks. Doses in female rats and male and female mice were 0, 125 and 250 mg/kg/day, 5 days/week. Male rats were treated at dosages of 0, 62 and 125 mg/kg/day, 5 days/week.

For rats, dose-related decreased body weight was observed in males and females throughout the study. At the end of the study, body weights were decreased below controls by 5% for low-dose males and females, 14% for high-dose males and 24% for high-dose females. Females in the high-dose group also had significantly reduced survival ($p<0.001$) compared with controls (see Section 5.1.). After 105-108 weeks, the surviving rats were killed. Gross and comprehensive histologic examinations were performed on all rats that died or were killed when moribund during the study, as well as on rats that were killed at the end of the study. Treatment-related neoplastic changes occurred (see Section 5.1.). High-dose female rats had increased incidences of nonneoplastic liver lesions consisting of foci of clear cell changes (3/50 controls, 5/50 low-dose, 11/50 high-dose) and focal and centrilobular necrosis (2/50 control, 1/50 low-dose, 12/50 high-dose). No other treatment-related nonneoplastic changes were observed.

For mice, no differences in body weights were observed, but low- and high-dose female rats had significantly reduced survival ($p=0.035$) (see Section 5.1.) that was related to increased incidence of reproductive tract infections. It was not clear if an increased susceptibility to infections was treatment-related. Surviving mice were killed after 105-107 weeks. Gross and comprehensive histological examinations were performed on all mice. In addition to the increased incidences of adenomas and carcinomas of

the liver (see Section 5.1.), male mice had increased incidences of hepatocytomegaly (3/50 control, 5/49 low-dose, 15/50 high-dose) and focal and centrilobular hepatic necrosis (2/50 control, 5/49 low-dose, 10/50 high-dose). There were also increased incidences of acanthosis of the forestomach epithelium as follows: 2/49 high-dose males, 5/50 low-dose females and 4/50 high-dose females. Acanthosis was not observed in male or female controls or in low-dose males.

In 13-week studies, groups of 10 male and 10 female F344/N rats and B6C3F1 mice were treated by gavage with 1,2-dichloropropane (NTP, 1983). Doses in rats were 0, 60, 125, 250, 500 and 1000 mg/kg/day, 5 days/week. All rats treated with 1000 mg/kg/day and 5/10 male rats treated with 500 mg/kg/day died before the end of the study. Decreased body weight gain was observed in males and females at 500 mg/kg/day. At 1000 mg/kg/day, 5/10 males and 2/10 females had centrilobular congestion and 2/10 females had hepatic fatty changes and centrilobular necrosis. No other treatment-related effects were observed.

Doses in mice were 0, 30, 60, 125, 250 and 500 mg/kg/day, 5 days/week for 13 weeks (NTP, 1983). One female treated at 500 mg/kg/day and one male treated at 60 mg/kg/day died. No significant or dose-related body changes and no treatment-related histopathologic changes were observed.

In an inhalation study, Heppel et al. (1946) exposed rabbits, guinea pigs, rats and mice to 1,2-dichloropropane at 10.4 mg/ℓ (10,400 mg/m³) for 7 hours/day. Severe signs of CNS toxicity and deaths occurred within eight exposures. Mice died after one exposure. Rats, guinea pigs and rabbits were also exposed to 1,2-dichloropropane at 0 and 6.5 mg/ℓ (6500 mg/m³), 7 hours/day, 5 days/week for up to 39 exposures; rats, guinea

pigs, rabbits, puppies and dogs were exposed at 0 and 4.4 mg/ℓ (4400 mg/m³) for 7 hours/day, 5 days/week for up to 128 exposures. At 6500 mg/m³, increased numbers of deaths occurred among all species compared with controls, beginning at 2-3 weeks of exposure. The concentations of 6500 and 4400 mg/m³ were fatal to mice after single exposures for 2-4 hours. At 4400 mg/m³, increased mortality was observed in all species except rabbits; time to death was longer at the lower exposure. Signs of CNS toxicity in guinea pigs and rats, reduced growth rates in rats and anorexia in dogs were observed. Liver and kidney function tests were performed on dogs with negative results. Animals that died had congestion and fatty degeneration of the liver and kidney, and necrotic lesions in the liver. Guinea pigs that died also had histopathologic lesions in the adrenal cortex, and rats had marked hemosiderosis.

In another study, groups of 26 male and 23 female rats, 12 male and 20 female guinea pigs, 5 male dogs, 16 strain C57 mice of unspecified sex and 80 strain C3H mice of unspecified sex were exposed by inhalation to 1,2-dichloropropane at 400 ppm (1849 mg/m³), 7 hours/day, 5 days/week (Heppel et al., 1948). The rats, guinea pigs and dogs received 128-140 exposures over a period of ~28 weeks. No treatment-related deaths occurred in rats, guinea pigs or dogs. Reduced body weight gain was observed in male and female rats. No treatment related histopathologic changes were observed among these species, with the possible exception of slightly increased incidences of hemosiderosis in rats and guinea pigs and fatty changes in the adrenals of guinea pigs. All of the C57 mice died or were killed within 12 exposures. Histologic examination revealed slight fatty degeneration of the liver and kidney in some of these mice. The C3H mice received exposures for 4-7 hours/day for a total of 37 exposures. Mortality was high during the

exposures. Histological examination revealed congestion and fatty degeneration and centrilobular necrosis in the liver and fatty degeneration in the kidneys. Only three mice were still alive 7 months after the last exposure; all of these had multiple hepatomas (see Section 5.1.).

Sidorenko et al. (1979) exposed an unspecified number of rats continuously to 1,2-dichloropropane by inhalation at 0, 1.5, 9, 100, 500, 1000 or 2000 mg/m³. Rats exposed to 2000 and 1000 mg/m³ were killed after 168 hours; rats exposed to 500 and 100 mg/m³ were killed after 360 hours; and rats exposed to 9 and 1.5 mg/m³ were killed after 86 days. Body weight gain and hemotologic parameters were comparable among exposure groups. The onset of CNS system changes as indicated by a change in total threshold indicator (not otherwise defined) was measured at each exposure level. At 2000 mg/m³, significant ($p<0.05$) changes in total threshold indicator occurred at 48 hours of exposure; whereas, at 100 mg/m³, a significant change occurred at 360 hours. At 9 mg/m³, no significant change occurred until 2040 hours (85 days) of exposure. A significant change in blood catalase activity appeared after 4 hours of exposure at 2000 mg/m³, 12-120 hours at 1000 to 100 mg/m³ and 2040 hours at 9 mg/m³. Significant changes in blood cholinesterase activity appeared after 4 hours at 2000 mg/m³, 72 hours at 100 mg/m³ and 600 hours (25 days) at 9 mg/m³.

Changes in the lung included supression of oxidizing enzymes at 2000 mg/m³, induced "bioelectric process" activity at 1000 mg/m³ and elevated oxidizing enzymes in alveolar and bronchial epithelium and increased numbers of microphages at "low concentrations." Edema, osmiophillic corpuscles and increased reactivity of macrophages were seen by electron microscopy of lung sections of rats exposed to 9 mg/m³. Increasing ploidy in liver cells was observed at 1000 and 2000 mg/m³; lesser degrees of increased ploidy

occurred at 100 and 500 mg/m³. Slight decreases in RNA content and enzyme activity in the centrilobular area of the liver were observed at 9 mg/m³. Exposure to 1.5 mg/m³ produced slight increases in liver enzyme activities (not clearly specified) but no structural changes. Increased ploidy in liver cells as evidenced by increased DNA content was observed at $\geq$9 mg/m³. Similar results were reported in an abstract of a study from the same laboratory (Shaipak, 1976).

Belyaeva et al. (1977) exposed rats continuously to 9 mg/m³ of 1,2-dichloropropane for 3 months. Liver histochemical and morphological changes were observed in the centrilobular region.

5.6. OTHER RELEVANT INFORMATION

St. George (1937) described "marked anemia" with symptoms of headache, vertigo, lacrimation and mucous membrane irritation in cases of 1,2-dichloropropane poisoning in humans.

In a 46-year-old man who accidentially ingested 50 mL of a cleaning solution containing 1,2-dichloropropane, deep coma with mydriasis and hypertonia occurred after 2 hours. Consciousness was regained 24 hours after he had been treated by artificial ventilation and osmotic diuresis (Larcan et al., 1977). After 36 hours, however, irreversible shock, followed by death from cardiac failure with lactic acidosis and hepatic cytolysis occurred. Centri- and mediolobular necrosis was observed in the liver upon autopsy.

LD_{50} and LC_{50} values for dichloropropanes are summarized in Table 5-3. Wright and Schaffer (1932) administered dichloropropanes to dogs in a single oral dose of 5700 mg/kg. Loss of coordination and staggering occurred within 15 minutes, followed by complete lack of coordination after 90 minutes, and death at 3.5 hours after dosing. At an oral dose of 3500 mg/kg bw, staggering, partial narcosis and death occurred in 24 hours.

TABLE 5-3

LD_{50} and LC_{50} Values for Dichloropropane

Compound	Route	Species	LD_{50} or LC_{50}	Reference
1,2-Dichloropropane	oral	rat	2200 mg/kg	Smyth et al., 1969
1,2-Dichloropropane	oral	rat	2200 mg/kg	Ekshtat et al., 1975
1,2-Dichloropropane	oral	rat	1947 mg/kg	Pozzani et al., 1959
1,2-Dichloropropane	oral	guinea pig	200-4000 mg/kg	Anonymous, 1967
1,1-Dichloropropane	oral	rat	6500 mg/kg	Smyth et al., 1954
1,2-Dichloropropane	inhalation	rat	9924 mg/m³ 8 hours	Smyth et al., 1969
1,2-Dichloropropane	dermal	rabbit	10,200 mg/kg	Smyth et al., 1969
1,1-Dichloropropane	dermal	rabbit	16,400 mg/kg	Smyth et al., 1954

Necropsy revealed hypostatic congestion of the lungs, congestion of bladder and kidneys, and respiratory tract and stomach hemorrhages. Histopathologic lesions included congestion, severe cloudy swelling, fat accumulation, deposition of bile pigments in the liver and congestion and degeneration of the tubular epithelium in the kidney. Moderately severe lesions of the liver, GI tract and kidneys were also observed at 350 mg/kg bw.

Strusevich and Sadovnik (1975) reported increased blood trypsin and lipase activity following oral doses of 27.5 mg/kg of 1,2-dichloropropane at 5-day intervals for 15 days.

In 14-day studies, groups of five male and five female F344/N rats and B6C3F1 mice were treated by gavage with 1,2-dichloropropane at 0, 125, 250, 500, 1000 and 2000 mg/kg/day, 5 days/week for 2 weeks (NTP, 1983). All rats and mice at 2000 mg/kg/day, all male mice and 4/5 female mice at 1000 mg/kg/day and 3/5 male mice at 500 mg/kg/day died. Mean body weight of mice were comparable among groups, but male and female rats at 1000 mg/kg/day weighed 14-15% less than controls. At necropsy, reddened renal medullae were found in rats at 2000 mg/kg/day and in mice at $\geq$125 mg/kg/day. Histologic examinations were not performed.

Kurysheva and Ekshtat (1975) exposed rats to oral doses of 14.4 and 360 mg/kg bw of 1,2-dichloropropane for 30 days. Blood serum cholesterol, β-lipoproteins and γ-globin levels increased after day 10. By day 20, inhibition of serum cholinesterase was noted but levels of fructose-1-monophosphate aldolase, alanine transaminase and asparagine transaminase were increased. At 30 days, alanine transaminase was also inhibited.

In inhalation experiments, Highman and Heppel (1946) exposed rats and guinea pigs to 10,146 mg/m^3 of 1,2-dichloropropane for one 4-hour exposure or up to five 7-hour exposures. Controls consisted of 3-6 animals/species

that were not exposed to compound vapors. Exposed animals were sacrificed immediately after exposure, 16 hours after a 7-hour exposure or at intervals from 0-21 days following exposure. Histopathological effects on livers, kidneys and adrenal glands were observed in both species. In rats, centrilobular necrosis in the liver and fatty degeneration of both the liver and kidney was observed. In addition, necrosis of the adrenal cortex, persisting for 14-21 days was noted. Guinea pigs exhibited fatty livers and central hemorrhagic areas in the adrenals. Histologic lesions included fatty degeneration of the liver, coagulation in the kidney, focal hemorrhagic necrosis and congestion and fatty degeneration.

Sidorenko et al. (1976) exposed treated white mice by inhalation to 4800, 12,600, 17,500, 22,000 and 26,000 mg/m³ 1,2-dichloropropane for brief periods of unspecified duration. Decreased coordination, sluggishness, amyotonia and clonic spasms, followed by loss of the righting reflex were observed.

Albino male rats were exposed continuously by inhalation to 1000 and 2000 mg/m³ of 1,2-dichloropropane for 7 days (Sidorenko et al., 1976). As early as 4 hours of exposure to 1000 mg/m³, there were significant changes in catalase, cholinesterase and threshold index. After 7 days, protein and fat dystrophy, enzyme activity suppression, and decreased ribonucleoproteins were observed in centrilobular sections of the liver. Hyperplasia and hypertrophy of cellular and intracellular structures were observed in the periphery of the lobules. Polyploid hepatocytes increased in number. Similar changes were also noted in the kidney. Structural changes were seen in the proximal convoluted tubules, loops of Henle, and medullar zone collecting tubules.

Belyaeva et al. (1977) exposed rats continuously by inhalation to 1100 mg/m³ of 1,2-dichloropropane for 1 week. Histochemical and morphological changes were observed in central portions of the liver.

Bonashevskaya et al. (1978) exposed rats to 1 or 2 mg/m³ continuously for 7 days. Extensive lung hemorrhages and destruction of bronchial, bronchiolar and alveolar epithelium occurred along with inhibition of lung enzymes.

Drew et al. (1978) found that exposure of rats by inhalation to 1,2-dichloropropane at 1000 ppm (4621 mg/m³) for 4 hours resulted in significantly increased activities of SGOT and SGPT and decreased activity of glucose-6-phosphatase within 0-1 day of exposure, compared with preexposure activities.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The acute toxicity of dichloropropanes has been examined by a number of researchers in freshwater and marine fish and aquatic invertebrate species. In tests to identify a lampricidal compound, Applegate et al. (1957) reported no mortality in larval lampreys, Petromyzon marinus, rainbow trout, Salmo gairdneri or bluegill sunfish, Lepomis macrochirus, following 24-hour exposures to 5.0 mg 1,3-dichloropropane/ℓ. Schneider (1979) reported 24-, 48- and 96-hour LC_{50} values of 8.8, 7.2 and 5.9 mg 1,3-dichloropropane/ℓ, respectively, in rainbow trout. Dawson et al. (1977) reported that 1,2-dichloropropane caused 100% mortality within 24 hours in bluegill sunfish exposed at 560 mg/ℓ, while levels of 320 and 180 mg/ℓ caused 40% and 0% mortality, respectively. When tests were conducted for 96 hours, the test-fit LC_{50} was 320 mg 1,2-dichloropropane/ℓ in bluegills. The 24-, 48-, 72- and 96-hour LC_{50} values for 1,2-dichloropropane in the fathead minnow, Pimephales promelas, were 194, 154, 141 and 140 mg/ℓ, respectively (Walbridge et al., 1983). Bridie et al. (1979b) reported a 24-hour LC_{50} at 160 mg 1,3-dichloropropane/ℓ in goldfish, Carassius auratus.

The U.S. EPA (1978) conducted a battery of toxicity tests of 1,1-, 1,2- and 1,3-dichloropropane in aquatic species. In bluegill sunfish, L. macrochirus, 24-, 48-, 72- and 96-hour LC_{50} values were all 97.9 mg/ℓ for 1,1-isomer and >520 mg/ℓ for 1,3-dichloropropane. The 24-, 48-, 72- and 96-hour LC_{50}s for 1,2-dichloropropane were 359, 318, 291 and 280 mg/ℓ, respectively, in the bluegill (U.S. EPA, 1978; Buccafusco et al., 1981). NOECs were <46, <36 and <112 mg/ℓ for 1,1-, 1,2- and 1,3-dichloropropane, respectively. In the marine sheepshead minnow, Cyprinodon variegatus, only 1,3-dichloropropane was tested, having an LC_{50} value of 86.7 mg/ℓ for all time periods up to 96 hours and a NOEC of 38.4 mg/ℓ (U.S.

EPA, 1978; Heitmuller et al., 1981). Mortality in the tidewater silverside, Menidia beryllina, was determined during 96-hour tests of 1,2-dichloropropane at 100, 180, 240 and 320 mg/ℓ to determine the best-fit LC_{50} (Dawson et al., 1977). The 96-hour LC_{50} was determined to be 240 mg/ℓ.

Tests by the U.S. EPA (1978) were also conducted in the freshwater crustacean, Daphnia magna, and the marine shrimp, Mysidopsis bakia. In daphnids the 24- and 48-hour LC_{50} values were 30.3 and 23.0, 99.3 and 52.5, and 487 and 282 mg/ℓ, respectively, for 1,1-, 1,2- and 1,3-dichloropropane. The NOEC values were <6.8, <22 and 68 mg/ℓ for the respective isomers (U.S. EPA, 1978; LeBlanc, 1980). The 24-, 48-, 72- and 96-hour LC_{50} of 1,3-dichloropropane for the marine shrimp were 27.5, 31.3, 23.6 and 10.3 mg/ℓ, respectively. The NOEC was 0.37 mg 1,3-dichloropropane/ℓ. Hermens et al. (1984) reported that the 48-hour EC_{50} for immobilization of Daphnia magna was 37 mg/ℓ.

6.2. CHRONIC EFFECTS

Konemann (1981) reported 7-day LC_{50} values of 95 and 69 mg/ℓ for 1,2- and 1,3-dichloropropane, respectively in the guppy, Poecilia reticulata. The U.S. EPA (1978) reported a MATC between 2.2 and 4.2 mg 1,3-dichloropropane/ℓ. This level is based on toxic effects in mysid shrimp (the most sensitive species tested) during 96-hour tests.

In 32-day early life stage toxicity tests with fathead minnows, Pimephales promelas, Benoit et al. (1982) reported severely decreased larval survival at $\geq$25 mg 1,2-dichloropropane/ℓ and $\geq$65 mg 1,3-dichloropropane/ℓ. Growth of larvae was even more sensitive, showing significantly ($p>0.05$) reduced body weights at 11 and 16 mg/ℓ, respectively, for 1,2- and 1,3-dichloropropane. Based upon these studies, Benoit et al. (1982) estimated MATC levels of 6-11 mg/ℓ for 1,2-dichloropropane and 8-16 mg/ℓ for 1,3-dichloropropane.

6.3. PLANT EFFECTS

Toxicity tests of 1,3-dichloropropane using the freshwater algae, Selenastrum capricornutum, were conducted by the U.S. EPA (1978). The 24-, 48-, 72- and 96-hour EC_{50} values for growth inhibition were 108, 73.6, 73.4 and 48.0-72.2 mg/ℓ, respectively. The NOEC was <6.7 mg/ℓ. Toxicity levels for the marine algae, Skeletonema costatum, were within the same range. The 24-, 48-, 72- and 96-hour EC_{50} values for 1,3-dichloropropane were 99.7, 110, 606 and 65.8-93.6 mg/ℓ, respectively. The NOEC was determined to be 120 mg 1,3-dichloropropane/ℓ.

6.4. RESIDUES

Data regarding the residue of dichloropropane in aquatic organisms or the aquatic environment were not located in the available literature cited in the Appendix. Data regarding the fate of dichloropropanes in water was discussed in Chapter 2.

6.5. OTHER RELEVANT INFORMATION

Additional data pertinent to the toxicity of dichloropropanes to aquatic species were not located in the available literature as cited in the Appendix.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The ACGIH (1984) adopted a TWA-TLV of 75 ppm (350 mg/m³) and an STEL of 110 ppm (510 mg/m³) for occupational exposure to 1,2-dichloropropane. The TLV was derived from the studies of Heppel et al. (1946, 1948) (see Section 5.5.) as documented by the ACGIH (1980). Recommendations are 75 ppm (350 mg/m³) for most Western European nations, 40 ppm (185 mg/m³) for Romania, 10 ppm (46 mg/m³) for East Germany and Poland, and 2 ppm (9 mg/m³) for the USSR and Bulgaria (ACGIH, 1980). The TLV adopted by OSHA is also 75 ppm (350 mg/m³) (Code of Federal Regulations, 1981). U.S. EPA (1980a) determined that the data base at that time was inadequate to develop a health based criterion.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of dichloropropane were not located in the available literature as cited in the Appendix. The U.S. EPA (1980a) stated that acute and chronic toxicity to freshwater aquatic life occur at concentrations of dichloropropanes as low as 23,000 and 5,700 µg/l respectively, and would occur at lower concentrations among species that are more sensitive. For saltwater aquate life, acute and chronic toxicity occur at concentrations as low as 10,300 and 3,040 µg/l, respectively, and would occur at lower concentrations among species more sensitive than those tested. No criteria levels were estimated.

In the NTP (1983) study, rats treated by gavage with 1,2-dichloropropane 5 days/week for 103 weeks, had reduced body weights as follows (expressed as percentage of control): 5% for males at 62 mg/kg/day and females at 125 mg/kg/day, 14% for males at 125 mg/kg/day and 24% for females at 250

mg/kg/day. High-dose females also had significantly reduced survival and increased incidences of liver lesions (clear cell changes, focal and centrilobular necrosis). In mice similarly treated at 125 and 250 mg/kg/day, females had significantly reduced survival that was related to increased incidences of reproductive tract infections, and males had dose-related increased incidences of hepatocytomegaly and focal and centrilobular liver necrosis.

In a 13-week gavage study, survival and body weight were reduced at doses $\geq$500 mg/kg/day, 5 days/week, and histopathologic lesions were observed at 1000 mg/kg/day in rats (NTP, 1983). In mice, one female at 500 mg/kg/day and one male at 60 mg/kg/day died, but it was uncertain if the deaths were attributable to treatment. Therefore, 62 mg/kg/day, 5 days/week in the 2-year study, in which male rats had a 5% higher reduction of body weight, is the NOAEL for chronic oral exposure. Higher doses were associated with reduced survival and tumors.

In inhalation studies, exposures of 6500 mg/m^3, 7 hours/day, 5 days/week were fatal to rabbits and $\geq$4400 mg/m^3, 7 hours/day, 5 days/week were fatal to rats, guinea pigs and dogs, beginning at approximately the second week of exposure (Heppel et al., 1946). Mice were more sensitive, with

deaths occurring at 1849 mg/m³, 4-7 hours/day within 12 exposures and at ≥4400 mg/m³, 2-4 hours/day after a single exposure (Heppel et al., 1946, 1948). Histopathologic lesions were observed in kidneys, livers and adrenal of animals that died.

In Russian studies, continuous inhalation exposure of rats to 9 mg/m³ 1,2-dichloropropane for ~3 months was associated with changes in the "total threshold indicator" for CNS effects, changes in blood catalase activity and decreased RNA content, enzyme activity and ploidy in the liver (Sidorenko et al., 1979; Shaipak, 1976; Belyaeva et al., 1977). At higher concentrations (≥100 mg/m³), effects occurred sooner and were more severe. At 1.5 mg/m³, the only effect was a slight change in liver enzyme activities (Sidorenko et al., 1979).

Although the NOAEL for chronic oral exposure to 1,2-dichloropropane is 62 mg/kg/day, 5 days/week, at which male rats had slightly reduced (5%) body weight gain (NTP, 1983), it is inappropriate to derive an ADI because there is evidence that 1,2-dichloropropane is carcinogenic to rodents.

8. RISK ASSESSMENT

1,2-Dichloropropane has been shown to be positive, marginally positive and negative for reverse mutations in Salmonella typhimurium strains TA100 and TA1535. Generally the response was reduced or eliminated by the addition of S-9. Uniformly negative responses were obtained with other Salmonella strains. Positive responses were obtained for forward mutations in Aspergillus nidulans and for SCE and chromosome aberrations in mammalian cell systems (see Table 5-2). Metabolic activation was not required for the positive responses. Negative responses were reported for forward mutations in Streptomyces coelicolor. 1,3-Dichloropropane was also positive for reverse mutation in S. typhimurium strain TA100 (Stolzenberg and Hine, 1980).

Pertinent data regarding the teratogenicity of the dichloropropanes were not located in the available literature as cited in the Appendix. The only information regarding other reproductive effects of dichloropropanes was from an abstract of a Russian study (Shaipak, 1976) in which impaired spermatogenesis was observed in rats exposed by inhalation to 9 mg/m³ of 1,2-dichloropropane for "long periods of time."

Carcinogenicity and long-term toxicity data were available only for 1,2-dichloropropane. Treatment of female rats by gavage with 1,2-dichloropropane at 0, 125 and 250 mg/kg/day, 5 days/week for 103 weeks resulted in a significant dose-related increased incidence of adenocarcinomas of the mammary gland (NTP, 1983). Similar treatment of mice resulted in significant dose-related increased incidences of adenomas and incidences of adenomas or carcinomas of the liver in males and females. No treatment-related increased incidences of tumors were observed in male rats treated at 0, 62 or 125 mg/kg/day, 5 days/week. The results of the NTP (1983) study

TABLE 8-1

Cancer Data Sheet for Derivation of q_1^*

Compound: 1,2-dichloropropane

Reference: NTP, 1983

Species, Strain, Sex: mouse, B6C3F1, male

Body weight: 0.04 kg (measured)

Length of Exposure (le) = 103 weeks

Length of Experiment (Le) = 105-107 weeks

Lifespan of Animal (L) = 105-107 weeks

Tumor Site and Type: liver, adenoma or carcinoma

Route, vehicle: gavage, corn oil

Experimental Doses or Exposures (mg/kg/day, 5 days/week)	Transformed Dose (mg/kg/day)	Incidence No. Responding/No. Tested
0	0	18/50
125	86.8	25/49
250	173.5	32/50

Unadjusted q_1^* from study = 5.2542533×10^{-3} $(mg/kg/day)^{-1}$
Human q_1^* = 6.331749×10^{-2} $(mg/kg/day)^{-1}$

TABLE G-2

Cancer Data Sheet for Derivation of q_1^*

Compound: 1,2-dichloropropane

Reference: NTP, 1983

Species, Strain, Sex: mouse, B6C3F1, female

Body weight: 0.038 kg (measured)

Length of Exposure (ℓe) = 103 weeks

Length of Experiment (Le) = 105-107 weeks

Lifespan of Animal (L) = 105-107 weeks

Tumor Site and Type: liver, adenoma or carcinoma

Route, vehicle: gavage, corn oil

Experimental Doses or Exposures (mg/kg/day, 5 days/week)	Transformed Dose (mg/kg/day)	Incidence No. Responding/No. Tested
0	0	1/50
125	86.8	7/50
250	173.5	9/50

Unadjusted q_1^* from study = 1.8363078×10^{-3} $(mg/kg/day)^{-1}$
Human q_1^* = 2.2510422×10^{-2} $(mg/kg/day)^{-1}$

are summarized in Table 5-1. All three mice that survived a 7-month observation period following inhalation exposure of 80 mice to 1,2-dichloropropane at 1849 mg/m³ for 4-7 hours/day for a total of 37 exposures had multiple hepatomas (Heppel et al., 1948).

The evidence for the increased incidence of mammary gland adenocarcinomas in female rats is equivocal; however, the increased incidence of adenoma in the liver of male and female mice provided some evidence for carcinogenicity (NTP, 1983), and the incidence of carcinomas in the liver support the evidence. Therefore it is appropriate to derive a q_1^* from the incidence data for adenoma or carcinoma of the liver. Dose-related increased incidences of these tumors were found in both male and female mice (see Table 5-1). Data used to calculate the q_1^* values are summarized in Tables 8-1 and 8-2. The transformed doses were calculated by multiplying the experimental doses of 125 and 250 mg/kg/day by 5 days/7 days and by 103 weeks/106 weeks (106 weeks is the average length of the experiment). The unadjusted q_1^* values were derived using the linearized multistage model developed by Kenneth Crump and adopted by the U.S. EPA (Federal Register, 1980). The chi-square analysis indicated that the goodness-of-fit for the data for females was adequate; no chi-square analysis of the data for males could be performed because there were zero degrees of freedom. The q_1^* values for humans were calculated by multiplying the unadjusted value by the cube root of the ratio of the body weight of a man (assumed to be 70 kg) to the average weight of the mice (0.04 kg for males, 0.038 kg for females). The q_1^* values are 6.33×10^{-2} $(mg/kg/day)^{-1}$ obtained from the data for males and 2.25×10^{-2} $(mg/kg/day)^{-1}$ obtained from the data for females. Since the q_1^* of 6.33×10^{-2} $(mg/kg/day)^{-1}$ for males is higher, it is recommended for estimating the increased lifetime cancer risk for exposure

to 1,2-dichloropropane. The same value for q_1^* was derived previously (U.S. EPA, 1984a).

As emphasized by U.S. EPA (1984a), the risk assessment was based on data from a draft report of the NTP (1983) study that is undergoing audit. The draft that was available during the preparation of the U.S. EPA Drinking Water Criteria Document was dated May, 1983; the draft that was used in the current risk assessment was dated December, 1983. No substantial differences between the two drafts were apparent. A final report of the bioassay on 1-2-dichloropropane has not been published.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

The available data on the effects of long-term exposure of animals to 1,2-dichloropropane were discussed in Section 5.5. No long-term studies of 1,1- or 1,3-dichloropropane were located. Data used to calculate CSs are presented in Table 9-1.

In addition to the data on the carcinogenicity of 1,2-dichloropropane (see Section 5.1.), the NTP (1983) gavage study provided information on other toxic effects of chronic and subchronic oral exposure to dichloropropane. Since data are available for chronic exposure (103 weeks), the 13-week studies need not be considered for RQ derivation. Reduced body weight gain was observed in male and female rats. At a dose of 62 mg/kg/day, the lowest dose in the study, male body weight was reduced 5% compared with control. The human MED of 554.4 mg/day is calculated by multiplying the rat dose of 62 mg/kg/day by 5/7 to expand the dose over the entire week, by the cube root of the rat weight (~0.4 kg for low-dose males in the study) to the weight of a man (70 kg) and by 70 kg. The MED corresponds to an RV_d of 1.4. The effect of reduced body weight warrants an RV_e of 4. The CS of 5.6 is obtained by multiplying the RV_e by the RV_d. The RQ corresponding to the CS of 5.6 is 1000.

In the NTP (1983) study, high-dose (250 mg/kg/day) female rats and low- and high-dose (125 and 250 mg/kg/day) male mice had increased incidences of centrilobular necrosis in the liver. Low- and high-dose female mice (125 and 250 mg/kg/day) and high-dose male mice had acanthosis of the forestomach epithelium. Survival was markedly reduced in both groups of female mice and in high-dose female rats. The reduced survival of the mice was attributed to increased incidences of reproductive tract infections, but it was not

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TABLE 9-1

Composite Scores for the Toxicity of 1,2-Dichloropropane

Route	Species	Dose/Exposure	Human MED (mg/day)	RV_d	Effects	RV_e	CS	RQ	Reference
Oral	rat	62 mg/kg/day, 5 days/week (44.3 mg/kg/day) 103 weeks	554.4	1.4	Reduced body weight	4	5.6	1000	NTP, 1983
Oral	mouse	125 mg/kg/day, 5 days/week (89.3 mg/kg/day) 103 weeks	509.9	1.4	Reduced survival, liver necrosis	10	14	1000	NTP, 1983
Inhalation	rat	9 mg/m³ continuous for 85 days	6.9*	4.3	Decreased total threshold indicator for CNS changes increased activities of enzymes in lung and liver changes in the reactivity and ultrastructural changes in alveolar macrophage system; increased ploidy in liver cells	3	12.9	1000	Sidorenko et al., 1979
Inhalation	rat	1.5 mg/m³ continuous for 85 days	1.1*	5.4	Increased activity of liver enzymes	1	5.4	1000	Sidorenko et al., 1979

*The exposures were divided by an uncertainty factor of 10 to approximate chronic exposure.

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certain if greater susceptibility to infection was a treatment-related effect. Nevertheless, the lowest human MED is calculated from the data for the reduced survival of low-dose female mice because female mice had the lowest body weight (0.038 kg). The dose of 125 mg/kg/day, 5 days/week is expanded to 7 days/week to 89.3 mg/kg/day, multiplied by the cube root of the body weight ratio and by 70 kg to give an MED of 509.9 mg/day, corresponding to RV_d of 1.4. Reduced survival has the maximum RV_e of 10. The CS is 14 and the RQ is 1000.

Data regarding the effects of inhalation exposure to 1,2-dichloropropane are from the studies of Heppel et al. (1946, 1948) and the Russian study (published in English) by Sidorenko et al. (1976). As discussed in previous determinations of the RQ for dichloropropanes (U.S. EPA, 1983a,b), the studies of Heppel et al. (1946, 1948) are not adequate for RQ derivations, since the lowest concentration tested, 400 ppm or 1849 mg/m³, resulted in the death of mice after a few exposures for 4-7 hours/day.

In the study by Sidorenko et al. (1979), only the 1.5 and 9 mg/m³ continuous exposures were continued for 85 days. At 9 mg/m³, the total threshold indicator for CNS effects (not further defined) in rats was decreased and activities of enzymes and RNA content in lung and liver were increased. There were also changes in the reactivity and ultrastructural changes in the alveolar macrophage system, and ploidy of liver cells was increased. At 1.5 mg/m³, increased activity of liver enzymes was found. The exposures of 9 and 1.5 mg/m³ are converted to animal doses of 5.7 and 0.96 mg/kg/day, respectively, by multiplying by a rat 24 hours breathing volume of 0.223 m³ and by dividing by a rat body weight of 0.35 kg. The doses are converted to MEDs by multiplying by the cube root of the body weight ratio of rats: human, multiplying by 70 kg and dividing by an

uncertainty factor of 10 to approximate chronic exposure. The Rvds are 4.3 and 5.4, respectively. Since very few data were tabulated, methods were not. described, the endpoints of total threshold indicator were not defined, the highest RV_e that can be assigned for the effects at 9 mg/m³ is 3. The increased liver enzyme activities at 1.5 mg/m³ warrant an RV_e of 1. CSs for the two exposures are 12.9 and 5.4, both corresponding to an RQ of 1000.

As seen from Table 9-1, the highest CS was obtained for the data regarding reduced survival of female mice in the NTP (1983) study, which is recommended as the basis for the RQ for 1,2-dichloropropane (Table 9-2). No data were available for 1,1-dichloropropane; the RQ for 1,2-dichloropropane may also apply for these isomers.

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Available data regarding the carcinogenicity of 1,2-dichloropropane were discussed in Section 5.1. No data for 1,1- and 1,3-dichloropropane were located. As seen in Table 5-1, treatment of female rats with 1,2-dichloropropane by gavage at 0, 125 and 250 mg/kg/day, 5 days/week for 103 weeks resulted in a significant dose-related increased incidence of mammary gland adenocarcinoma. The incidence in the high-dose group was significantly greater than the control when analyzed by the Life Table Tests. The Life Table Test was considered the most meaningful analysis because of the reduced survival of the high-dose females. No treatment-related increased incidence of tumors was found in male rats treated at 0, 62 and 125 mg/kg/day, 5 days/week.

For mice, there were significant dose-related increased incidences of adenoma and adenoma or carcinoma of the liver of males and females. The increased incidence of carcinoma considered alone was not significant. NTP

TABLE 9-2

1,2-Dichloropropane

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	oral
Dose*:	509.9 mg/day
Effect:	reduced survival
Reference:	NTP, 1983
RV_d:	1.4
RV_e	10
Composite Score:	14
RQ:	1000

*Equivalent human dose

(1983) concluded that the evidence for carcinogenicity in female rats was equivocal, but the incidence data for adenoma of the liver provided some evidence that 1,2-dichloropropane was carcinogenic to mice. The increased incidence of carcinomas supports the conclusion.

In an inhalation study, only 3/80 mice that had been exposed to 1,2-dichloropropane for 4-7 hours/day for a total of 37 exposures survived the 7-month observation period (Heppel et al., 1948). All three survivors had multiple hepatomas. It is difficult to draw conclusions from this study because of the low survival and lack of control data.

Based on the IARC criteria for weight of evidence for carcinogenicity, there is somewhat limited evidence that 1,2-dichloropropane could be carcinogenic to humans. No direct data regarding the carcinogenicity of 1,2-dichloropropane to humans are available. Positive carcinogenic evidence has been demonstrated in mouse liver (male and female) and rat mammary gland (female). Therefore, 1,2-dichloro- propane is placed in Group 2B. This would correspond to Group B2, possible human carcinogen, applying proposed U.S. EPA (1984b) guidelines.

To calculate the $1/ED_{10}$, the linearized multistage model developed by Kenneth Crump and adopted by the U.S. EPA (Federal Register, 1980) was used. The data used to calculate the $1/ED_{10}$ and F factor are shown in Table 9-3; the data for male mice resulted in the most conservative values. The doses of 125 and 250 mg/kg/day, 5 days/week were transformed to 86.8 and 173.5 mg/kg/day, respectively, by multiplying by 5/7 to expand the exposure over the entire week and by 103 weeks (the duration of treatment) divided by 106 weeks (the midpoint of the duration of the study). The unadjusted $1/ED_{10}$ of 2.79×10^{-2} $(mg/kg/day)^{-1}$ was converted to the F factor of 3.37×10^{-1} $(mg/kg/day)^{-1}$ by multiplying by the cube root of the ratio of the human weight (70 kg) to the weight of the male mice (0.04 kg).

Since the F factor is <1, it is placed in potency group 4. A potency group 4 chemical with an IARC classification of 2B has a LOW Hazard Ranking under CERCLA.

TABLE 9-3

Derivation of Potency Factor (F)

Agent: 1,2-dichloropropane

Reference:	NTP, 1983
Exposure Route:	oral
Species:	mouse
Strain:	B6C3F1
Sex:	male
Vehicle or Physical State:	corn oil
Body Weight:	0.04 kg
Duration of Treatment:	103 weeks
Duration of Study:	105-107 weeks
Lifespan of Animal:	105-107 weeks
Target Organ:	liver
Tumor Type:	adenoma or carcinoma
Experimental Doses/Exposure:	0, 125, 250 mg/kg/day, 5 days/week
Transformed Doses (mg/kg/day):	0, 86.8, 173.5
Tumor Incidence:	18/50; 25/49; 32/50
Unadjusted $1/ED_{10}$:	2.7937495×10^{-3}
F Factor:	3.3666669×10^{-3}

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in December 1984. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

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Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

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Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Service Resource Publ. 137. Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California. State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. PB-269605. Prepared for the U.S. EPA, Washington, DC.

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